

Amendments to the Drawings:

The attached single sheet of drawings include changes to Figs. 11A and 11B:

Sheet 1, which includes Figs. 11A and 11B, replaces the sheet that includes Figs. 11A and 11B.

Attachment: One replacement sheet.

REMARKS

After entry of the amendments and remarks herein claims 117-134 will be pending in the application. Claims 1-116 were cancelled. New claims 117-134 were herein added. Amendments to the claims should in no way be construed as acquiescence to any of the Examiner's rejections and were made solely to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s). Support for the new claims is found throughout the specification and claims as originally filed. For example, support for independent claim 117 is found in claims 1, 9-12, 25, 27, 87 and 88; p. 8, line 18 to page 9, line 7; p. 10, lines 7-27; p. 15, lines 7-12; and Fig. 11. Support for dependent claims 118-134 is found in original claims 2-89. No new matter is added.

Interview Summary

Applicant's representatives thank Examiner Beisner for his time and helpful discussion in the in-person interview of October 17, 2006. Examiner Beisner and Applicant's representatives, Alexandra Jones and Jeffrey Kopacz, participated in the interview. The interview concerned the substance of the outstanding Office Action, and is summarized herein.

Objections

The Examiner has objected to the drawings. The Examiner argues that "all of the claimed structures encompassed by claims 1 – 8, 11 – 18, 21 – 30, 87 – 89, 93 – 95, 97 – 101 and 109 – 116 must be shown or the feature(s) canceled from the claim(s)." (Office Action, p.3).

As noted above claims 1-116 are cancelled. A corrected drawing showing the structures of the currently claimed invention is herein submitted. Specifically, the corrected drawing illustrates that the non-planar elements are an integral part of the microfluidic chip and have a surface defining the opening which comprises portions of a wall of a cell chamber.

The corrected drawings are supported by the specification and claims as originally filed including claims 1-89; p. 8, line 18 to page 9, line 7; p. 10, lines 7-27; p. 15, lines 7-12; and Fig. 11. Applicants respectfully request that the objection be withdrawn.

Claim Rejections- 35 U.S.C. § 112

Claims 1 – 8, 11 – 18, 21 – 30, 87 – 89, 93 – 95, 97 – 101 and 109 – 116 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. The Examiner argues that in claim 1 is “not clear how the additionally recited ‘one channel’, ‘fluid source’, ‘cell chamber’ and ‘at least one nonplanar element’ structurally cooperate with the previously positively recited elements . . . Also, which of the two recited at least one nonplanar elements is an integral part of the substantially planar substrate?”

Claims 2-8, 11-18, 21-30, 87-89, 94, 97, 98, 100, 101 and 109-116 are rejected as being indefinite in view of their dependency from claims 1, 93, 94 or 99.

Claim 24 is rejected for reciting “cell chamber” as it being unclear how it differs, if at all, from claim 1.

Applicants disagree with the Examiner, but have herein deleted the rejected claims. New claims 117-134 are believed to address the above discussed rejections. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1 – 8, 11 – 18, 21 – 30, 87 – 89, 93 – 95, 97 – 101 and 109 – 116, under 35 U.S.C. § 112, second paragraph.

Claim Rejections- 35 U.S.C. § 102

Claims 1 – 6, 11 – 18, 21 – 30, 87 – 89, 93 – 95, 97 – 101 and 109-116 are rejected under 35 U.S.C. § 102(a) or 102(e) as being anticipated by Baumann et al. (US 6,368,851). The Office Action states that the US 6,368,851 reference (“the ‘851 reference”) “discloses a substantially planar substrate (4) in communication with at least one conducting element (18), wherein the substantially planar substrate (4) comprises at least one nonplanar element (20) for establishing and/or maintaining electrical communication with a cell (3), at least one channel (38) in communication with a fluid source (See column 16, line 28, to column 17, line 2), at least one cell chamber (2) (See Figure 17), and at least one nonplanar element (20) exposed to fluid flow from a fluid source (See column 16, line 67, to column 17, line 2), and wherein the nonplanar element (20) is an integral part of the substantially planar substrate (4).” (Office Action, p.4)

Applicants respectfully traverse the rejection. However, in order to expedite prosecution, Applicants have herein cancelled claims 1-116 and added new independent claim 117 and

dependent claims 118-134 to more clearly define the claimed invention. The instantly claimed invention relates to a microfluidic chip. The microfluidic chip includes a cell chamber having at least one nonplanar element for establishing and/or maintaining electrical communication with a cell, wherein the nonplanar element has a surface defining an opening for separating a cell from an electrode compartment. The nonplanar element is an integral part of the microfluidic chip and its surface defining the opening is comprised of portions of the wall of the cell chamber. The microfluidic chip further includes a first channel that is lateral to the cell chamber and oriented so as to provide a positive fluidic pressure on a cell attached to the surface defining the opening of the non-planar element. A second channel is lateral to the cell chamber and in communication with the surface defining the opening on the wall of the cell chamber so as to produce a negative pressure on a cell, thus drawing it into contact with the surface defining the opening of the nonplanar element. The cell chamber, first and second channels are further defined as having two walls and a base. The walls are parallel to the height of said microfluidic chip and the base is perpendicular to the height of the microfluidic chip. Further, a high electrical resistance seal is established and/or maintained between the cell and the surface defining the opening by the combination of the positive pressure of the fluid flow from the first channel and the negative pressure from the second channel.

In order to anticipate a claim, each and every element of the claim must be found in a single reference. This is discussed in the Manual of Patent Examining Procedure § 2131:

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). “The identical invention must be shown in as complete detail as is contained in the . . . claim.” *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The elements must be arranged as required by the claim, but this is not an *ipsissimis verbis* test, i.e., identity of terminology is not required. *In re Bond*, 910 F.2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990).

The ‘851 reference does not anticipate the claimed invention as it fails to teach every element of the claimed invention. The ‘851 reference teaches a devise for automatically positioning a cell, via a suction pressure, on a protruding surface on the bottom of a well so as to measure a

variable state of the cell. Unlike the claimed invention the '851 reference does not address the problem of establishing and/or maintaining a high electrical resistance seal between a cell and a nonplanar element so as to reduce noise and increase signal. Specifically, the '851 reference fails to teach, *inter alia*, a (1) microfluidic chip; (2) nonplanar element on *the wall* of a cell chamber; (3) a first channel that provides a fluid flow with respect to the non-planar element so as to exert a positive fluidic pressure on a cell on the non-planar element; and (4) a high electrical resistant seal that is established and/or maintained between a cell and the surface defining the opening by the combination of the positive pressure fluid flow from the first channel and the negative pressure from the second channel.

The '851 reference does not teach a microfluidic chip. Furthermore, the '851 reference does not teach a first channel within the meaning of the instant claims. In the presently claimed invention, the first channel provides a fluid flow so as to exert a **positive pressure** on a cell on the nonplanar element. The '851 does not teach a channel with these capabilities. The Examiner argues that "the nonplanar element (20) [is] exposed to a fluid flow from a fluid source." (Office Action, p.4). However, the '851 reference does not disclose or suggest a channel which provides a fluid flow toward a cell and non-planar element. At best the '851 reference teaches a channel (e.g., more analogous to the second channel of the claimed intention, but still distinct), which provides a suction force (negative pressure) so as to pull the cell toward the nonplanar element. For example, Col 16, lines 28-39 of the '851 reference states:

In the embodiment according to FIG. 22, the inner cavity 16 of the measuring electrode 6 is connected to a liquid channel 38, which can be impinged by a controllable **partial vacuum**. The liquid channel 38 can, for this purpose, be connected to a micropump, for example, by which the nutrient medium 2 can be **sucked out** from the support area 5 of the specimen slide 4. In this way, the mounting of a cell 3 on the measuring electrode 6 is made easier. Optionally, after the supporting on the measuring electrode 6 of a cell that is suctioned via the liquid channel 38, a weak partial vacuum can be exerted on the cell 3 for a certain time period, until it automatically adheres to the support area 5.

Since the '851 fails to teach a channel which provides a positive pressure, it naturally fails to teach the establishment and/or maintenance of a high electrical resistant seal between a cell and a

nonplanar element via the combination of a positive pressure flow from a first channel and the negative pressure from a second channel.

Further, the presently claimed device has the non-planar element on **the wall** for the cell chamber of the cell chamber. The '851 patent does not teach the protruding surface on **the wall** of the cell chamber but rather on **the floor** of the cell chamber. The present claims define the orientation of the channels, nonplanar element and cell chamber with respect to the microfluidic device. As claimed it is clear that the cell chamber, first channel and second channel each have two walls and a base, and the walls are parallel to the height of the microfluidic chip and the base is perpendicular to the height of the microfluidic chip. Thus, the second channel and nonplanar element are in communication with the wall of the cell chamber and not the base (floor) as taught in the '851 patent. During the interview the Applicant's representatives and inventor Daniel Chiu discussed the advantages of having the nonplanar element on the wall rather than the base of a cell chamber in a microfluidic device. In brief, these advantages included ease of manufacture (e.g., etching the channels into the top of the chip rather than drilling of channels into the chip), maintaining a thin microfluidic chip size, and the ability to more easily control the length and width of the channel and therefore ease of controlling the resistance of the channel and the pressure applied to the cell.

In light of the above, Applicants request reconsideration and withdrawal of the rejection and allowance of the claims.

Claim Rejections- 35 U.S.C. § 103(a)

Claims 1 – 3, 5, 11-18, 21 – 23, 25, 27 – 30, 87 – 89, 93 – 95, 97 - 101, 109-113, 115 and 116 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Stett et al. (US 2003/0153067; WO 02/03058). The Office Action states that the '067 reference teaches:

a substantially planar substrate (31)...in communication with at least one conducting element (43), wherein the substantially planar substrate (31) comprises at least one nonplanar element (37) for establishing and/or maintaining electrical communication with a cell (11), at least one channel (45) in communication with a fluid source (See Figure 2), at least one cell chamber (16) (See Figure 2), and at least one nonplanar element (37) exposed to fluid flow from a fluid source (12 or 19). (Office Action, p.9).

The Examiner then goes on to state that the “[w]hile the reference disclosed that nonplanar element (37) is removable, claim 1 differs by reciting that the nonplanar element is integral with the substrate . . . absence of a showing of criticality and/or unexpected results, it would have been merely an obvious matter in design choice to provide the nonplanar element (37) of the primary reference as an integral structure of the substance when replacement of the element is not required. ” (Office Action; p.9-10)

Applicants respectfully traverse the rejection.

In order to expedite prosecution Applicants have herein cancelled the rejected claims and added new independent claim 117 and dependent claims 118-134. New claim 117 is herein added to more clearly define the claimed invention. The instantly claimed invention relates to a microfluidic chip. The microfluidic chip includes a cell chamber having at least one nonplanar element for establishing and/or maintaining electrical communication with a cell, wherein the nonplanar element has a surface defining an opening for separating a cell from an electrode compartment. The nonplanar element is an integral part of the microfluidic chip and its surface defining the opening is comprised of portions of a wall of said cell chamber. The microfluidic chip further includes a first channel that is lateral to the cell chamber and which is oriented so as to provide a positive fluidic pressure on a cell attached to the surface defining the opening of the nonplanar element. A second channel is lateral to the cell chamber and in communication with the surface defining the opening on the wall of the cell chamber so as to produce a negative pressure on a cell, thus drawing it into contact with the surface defining the opening of the nonplanar element. The cell chamber, first and second channels are further defined as having two walls and a base. The walls are parallel to the height of said microfluidic chip and the base is perpendicular to the height of the microfluidic chip. Further, a high electrical resistance seal is established and/or maintained between the cell and the surface defining the opening by the combination of the positive pressure of the fluid flow from the first channel and the negative pressure from the second channel.

The ‘067 reference alone or in combination with any of the other cited references does not render the present claims obvious. As was discussed during the interview, the ‘067 reference teaches a device for automatically selecting a cell from a population of cells and measuring an

electrical signal from the selected cell. In particular embodiments, the contact tip is coated with a ligand specific to a particular cell type. Unlike the claimed invention the '067 reference does not address the issue of establishing and/or maintaining a high electrical resistance seal between a cell and a nonplanar element so as to reduce noise and increase signal. Specifically, the '067 reference fails to teach a (1) a nonplanar element that is an integral component of the wall of a cell chamber; (2) a first channel that provides a fluid flow with respect to the non-planar element so as to exert a positive fluidic pressure on a cell on the non-planar element; and (3) a device that establishes and/or maintains a high electrical resistant seal between a cell and the surface defining the opening by the combination of a positive pressure of a fluid flow from a first channel and the negative pressure from the second channel.

The '067 reference does not teach a first channel within the meaning of the instant claims. In the presently claimed invention the first channel is oriented to provide a fluid flow with respect to the non-planar element so as to exert a positive pressure on a cell on the nonplanar element. The '067 does not teach a channel oriented to perform this function. The Examiner argues that "the nonplanar element (37) can be exposed to a fluid flow from a fluid source (12 or 19)." (Office Action, p.9). However, nowhere does the '067 reference disclose or suggest a first channel which is oriented so as to provide fluid flow with respect to the non-planar element so as to exert a **positive fluidic pressure on a cell attached to the surface defining the opening of the non-planar element.**

Since the '067 fails to teach a channel which provides a positive pressure, it naturally fails to teach the establishment and/or maintenance of a high electrical resistant seal between a cell and nonplanar element via the combination of a positive pressure flow from a first channel and the negative pressure from a second channel.

Further, the '067 reference does not teach the use of a nonplanar element that is an integral part of the wall of the cell chamber nor would it be obvious for one of skill in the art to make the contact tip an integral part of the wall of the '067 device in light of the teachings. For example, Applicants refer the Examiner, for example, to paragraphs [0024] – [0028] of the '067 published application which teach that the non-planar element is not integral. For example, at [0024] the specification teaches:

in a refinement of the apparatus, preference is given to the contact unit being arranged at the opening in a detachable manner, and further preference is given to the contact tip being arranged in a replaceable manner.

Furthermore, it would not be obvious to modify the '067 device so as to make the contact tip an integral part, as there is a need to use the contact tip in a detachable manner. This reasoning is evident in paragraph 25 of the '067 reference which teaches away for using an integral piece:

Advantageously, it is possible here to easily replace the contact unit and/or the contact tip, while the other components of the novel apparatus are reusable. **This measure is based on the finding that patch clamp tips can be used only once, and, after only a second use, the gigaseal is no longer sufficient and membrane perforation is no longer reliable.**

However, with the presently claimed invention it is preferable to have an integral nonplanar element that is not replaceable for the reasons discussed during the interview. These reasons include reproducibility of results, facilitation of parallelization, ease of use, and ease of manufacture (e.g., etching the channels into the top of the chip rather than drilling of channels into the chip).

In light of the above, Applicants respectfully request reconsideration and withdrawal of the rejection.

Claim 7 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Baumann et al. (US 6,368,851) or Stett et al. (US 2003/0153067 or WO 02/03058) in view of Klemic et al (Biosensor and Bioelectronics).

Claim 7 was herein cancelled. New claim 123 corresponds to cancelled claim 7. Applicants respectfully traverse the rejection for the reasons set forth above with respect to the rejection of the claims under 35 U.S.C. §102 (a)/(e) in light of Baumann et al. (US 6,368,851) and rejection of the claims under 35 U.S.C. §103(a) in light of Stett et al. (US 2003/0153067 or WO 02/03058). Klemic et al. does not cure the defects of Baumann et al. and Stett et al. In light of the above, Applicants respectfully request reconsideration and withdrawal of the rejection.

Claim 8 has been rejected under 35 U.S.C. § 103(a) as being unpatentable over Baumann et al. (US 6,368,851) or Stett et al. (US 2003/0153067 or WO 02/03058) in view of Maher et al (US 6,686, 193).

Claim 8 was herein cancelled. New claim 124 corresponds to cancelled claim 8. Applicants respectfully traverse the rejection for the reasons set forth above with respect to the rejection of the claims under 35 U.S.C. §102 (a)/(e) in light of Baumann et al. (US 6,368,851) and rejection of the claims under 35 U.S.C. §103(a) in light of Stett et al. (US 2003/0153067 or WO 02/03058). Maher et al. does not cure the defects of Baumann et al. and Stett et al. In light of the above, Applicants respectfully request reconsideration and withdrawal of the rejection.

Claim Rejections- Double Patenting

Claims 1-8, 11-18, 21-30, 87-89, 93-95, 97-101 and 109-116 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 31 – 37 and 62 of the copending Application No. 10/688,794. Applicants note that claims 1-116 are herein cancelled and new claims 117-138 are herein added. To the extent that a double patenting rejection applies to the new claims, Applicants submit that when the pending claims in the present application are indicated as allowable, Applicants will consider submitting, if appropriate, a terminal disclaimer complying with 37 C.F.R. §1.321 (b) and (c).

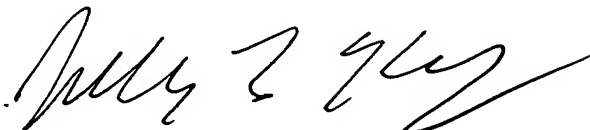
CONCLUSION

In light of the above remarks, Applicants respectfully request early consideration and allowance of the subject application.

Should the Examiner wish to discuss any of the amendments and/or remarks made herein, the undersigned attorney would appreciate the opportunity to do so.

The Commissioner is hereby authorized to charge any fees that may be required, or credit any overpayment to Deposit Account No. 04-1105.

Respectfully submitted,



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FIG. 11A

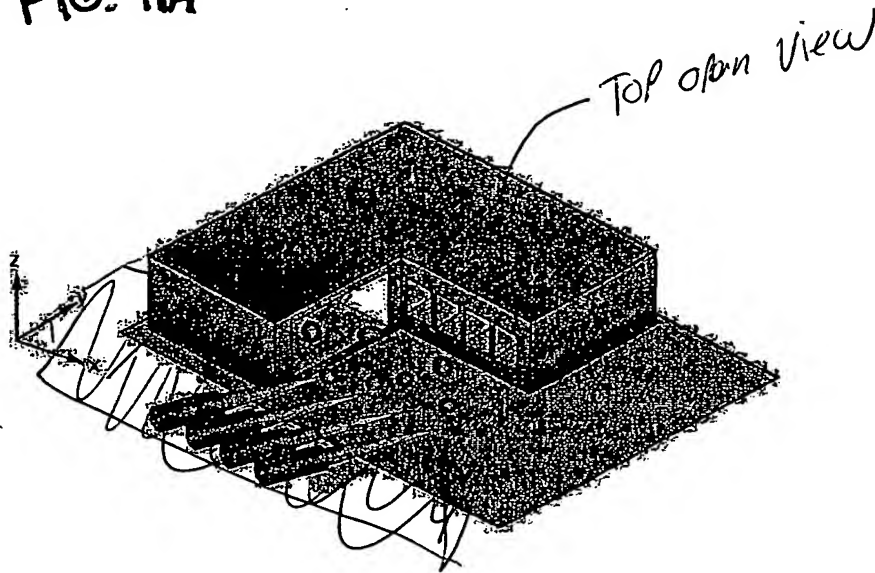
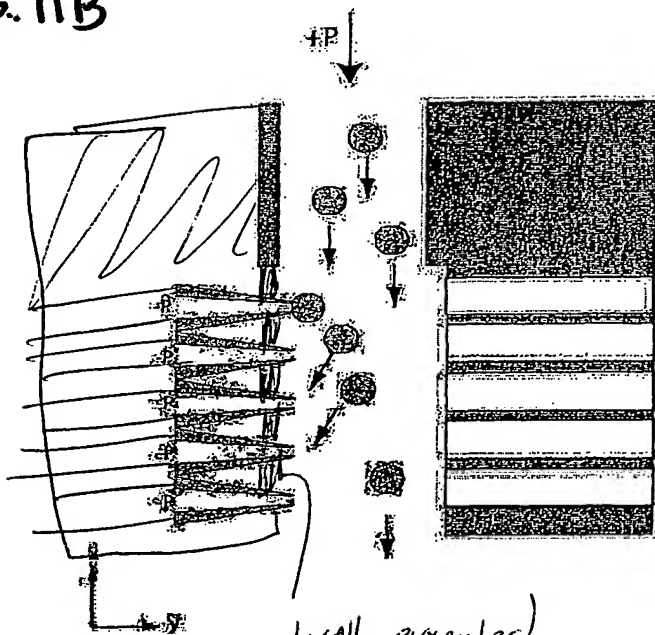


FIG. 11B



WALL extended
Non planar element IS Integral part of chip

Fig. 11